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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/587,642 | 04/16/2007 | Ana Gomez-Rodriguez | PLP574 | 4902 |

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| EXAMINER | |
|---|---|
| HINES, JANA A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1645 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 02/04/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/587,642 | GOMEZ-RODRIGUEZ ET AL. | |
| | Examiner | Art Unit | |
| | JaNa Hines | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-43 and 46-48* is/are pending in the application.

4a) Of the above claim(s) *10-13, 22-43 and 46-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/28/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of Group I in the reply filed on November 13, 2009 is acknowledged.

### *Information Disclosure Statement*

2. The information disclosure statement (IDS) submitted on July 18, 2006 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### *Specification*

3. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-9 and 14-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) The preamble of the claims is drawn to a method for generating and detecting recombinant DNA sequences in prokaryotes, however the recited steps within the method comprise a generation step; a cultivatling step and an isolation step. There is no correlation step which correlates the isolation of the second prokaryotic cell with detecting recombinant DNA. Therefore, the goal of the preamble is not commensurate with the steps of the method that are drawn to detecting recombinant DNA sequences.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 6 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a deposit rejection.

The specification lacks complete deposit information for the deposit of the *B. subtilis* plasmid pMIX91 comprising the $spec^R$ marker and the $phleo^R$ marker, the *B. subtilis* plasmid pMIX101 comprising the $tc^R$ marker, the *E. coli* plasmid pACYC184 or the *E. coli* plasmid pMIX100 or a derivative thereof. Because it is not clear that cell lines possessing the properties of the *B. subtilis* plasmid pMIX91 comprising the $spec^R$ marker and the $phleo^R$ marker, the *B. subtilis* plasmid pMIX101 comprising the $tc^R$

marker, the *E. coli* plasmid pACYC184 or the *E. coli* plasmid pMIX100 or a derivative thereof. are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of the *B. subtilis* plasmid pMIX91 comprising the $spec^R$ marker and the $phleo^R$ marker, the *B. subtilis* plasmid pMIX101 comprising the $tc^R$ marker, the *E. coli* plasmid pACYC184, the *E. coli* plasmid pMIX100 or a derivative thereof, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR

§1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the hybridoma cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundack, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-5, 7-9, 14 and 16-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al., ( Nature Genetics. 1998. Vol. 20: 123-128).

The claims are drawn to a method for generating and detecting recombinant DNA sequences in prokaryotes.

Zhang et al, teach homologous recombination presents an alternative way to engineer DNA, and a variety of approaches have been used in *E. coli*. These include recombination between independent replicons, for example, between a plasmid with a conditional replication origin and the *E. coli* genome[8], or a BAC (page 123). Alternatively, plasmid rescue by recombination between two linear DNA fragments has been. Recombination between linear DNA fragments and intact circular target molecules has also been described in *sbcB* and *recD* hosts (page 123). Zhang et al., teach the identification of a similarly flexible homologous recombination reaction in *E. coli*, we designed an assay on the basis of recombination between linear and circular DNA (page 123). Linear DNA carrying the Tn5 kanamycin resistance gene (*neo*) was made by PCR (Fig. 1a), using 60mer oligonucleotides consisting of 42 nt of homology to chosen regions in the plasmid and, at the 3' ends, 18-nt PCR primers (page 124). Linear and circular DNA were co-transformed into a variety of *E. coli* hosts. Homologous recombination was detected only in *sbcA* hosts (page 124). More than 95% of double ampicillin/kanamycin resistant colonies contained the expected homologously recombined plasmid, as determined by restriction digestion and sequencing (data not shown). A background of kanamycin resistance, due to genomic integration of *neo*, was very low (page 126). Homologous recombination presents an alternative way to engineer DNA, and a variety of approaches have been used in *E. coli*. These include recombination between independent replicons, for example, between a plasmid with a conditional replication origin and the *E. coli* genome[8], or a BAC (page 126-7). Alternatively, plasmid rescue by recombination between two linear DNA fragments has

been used (page 126). Recombination between linear DNA fragments and intact circular target molecules has also been described in *sbcB* and *recD* hosts (page 127). Zhang et al., teach homologous recombination is particularly flexible, and recombination between PCR fragments flanked by short homology arms and endogenous, intact recipients such as the yeast genome or YACs is routine (page 127). Zhang et al., teach the flexibility and reliability of ET cloning was explored by testing it in various contexts, and by combination with counterselection and site-specific recombination steps. The success of these experiments outlines a new logic for DNA engineering in *E. coli*.

Therefore Zhang et al., teach the instant claims.

***Claim Rejections - 35 USC § 102***

7. Claims 1-5, 7-8, 14, 16-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Peterson et al. (J Bacteriol. 1982 September; 151(3): 1086–1094).

The claims are drawn to a method for generating and detecting recombinant DNA sequences in prokaryotes.

Peterson et al., teach conjugation experiments were performed in which the donor was Escherichia coli K-12 strain KP245 containing either R plasmid NR1 plus an ampicillin-resistant derivative or NR1 plus RSF2124 carrying a cloned EcoRI fragment of NR1 (abstract). The recipient was the polA amber mutant JG112, in which RSF2124 cannot replicate. Ampicillin-resistant transconjugants can arise only when the genes for ampicillin resistance are linked to NR1 or are transposed to the host chromosome. Peterson et al., teach plasmid DNA from these ampicillin-resistant transconjugant cells

was analyzed by gel electrophoresis and was shown to be a cointegrate of NR1 and the RSF2124 derivative (abstract). Analysis of plasmid DNA isolated from donor cultures showed that the cointegrates were present before conjugation, which indicates that the mating does not stimulate cointegrate formation (page 1086). When the donor contained NR1 and RSF2124, the frequency of cotransfer of ampicillin resistance was less than 0.1%, and analysis of plasmid DNA from the ampicillin-resistant transconjugants showed that Tn3 had been transposed onto NR1 (page 1086).

Peterson et al., teach recombination between plasmids can result in the formation of cointegrate molecules in a cell. Cointegrate formation has been seen in *Escherichia coli* and *Bacillus subtilis* (page 1086). Cointegrate formation has also been observed between plasmids and bacteriophages (page 1986). In addition, in some cases, recA-independent cointegrate formation may be involved in the mobilization of nonconjugative plasmids (page 1086). Cointegrates were detected by mating from a donor containing the two plasmids to a polA recipient, in which RSF2124 cannot replicate (page 1086). The cointegrate nature of the plasmids was confirmed by genetic characterization of the ampicillin-resistant (Ap') transconjugants and by physical analysis of the plasmid DNA (page 1086). Peterson et al., teach cells from an overnight culture were grown (page 1087). Peterson et al, teach isolation and characterization of plasmid DNA. Plasmid DNA was isolated from stationary-phase cells and purified (page 1087). Cointegrate plasmid DNA was isolated from cells grown in the presence of ampicillin to select for their cointegrate structure (page 1087).

Therefore Peterson et al., teach the instant claims.

## *Conclusion*

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645